REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

I. Claim Amendments

By the foregoing amendments to the claims, claims 28, 32 and 34 have been amended as discussed below. Support for the amendments can be found throughout the application as filed.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

II. Response to Claim Rejections under 35 U.S.C. § 102 and/or § 103

Claims 21-23, 26-28, 38 and 39 have been rejected under 35 U.S.C. § 102(b) or (e) as allegedly being anticipated by WO 01/30812, U.S. Patent No. 7,285,539, or U.S. Patent No. 6,562,346 (each to Paliard et al.). In addition, or in the alternative, claims 29, 32, 34, 36-37, 39 and 40 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over the Paliard et al. references.

According to the Examiner, the Paliard et al. references each demonstrate that DNA encoding the HCV polypeptides NS3, NS4 and NS5b is immunogenic. In particular, the Examiner has stated that Example 11 in all three references explicitly teaches an expression vector encoding NS3NS4 and NS5b, which is used for priming the immune response against HCV, followed by a boost immunization with another plasmid encoding NS5a. This rejection is respectfully traversed.

The present claims are directed to expression vectors encoding HCV coding sequences, wherein the HCV coding sequences consist of a nucleotide sequence coding for a polyprotein NS3/NS4 of the hepatitis C virus, and a nucleotide sequence coding for a

polypeptide NS5b of the hepatitis C virus (see claim 21). The present expression vectors do not include nucleotide sequences coding for NS5a of the hepatitis C virus.

In contrast to the present claims, the Paliard et al. references teach the use of the NS5a polypeptide, and DNA encoding the same. Applicants submit that a person of ordinary skill in the art would recognize that the Paliard et al. compositions comprise the NS5a polypeptide. Furthermore, the skilled artisan would conclude that Example 11 does not teach or suggest an expression vector encoding only NS3NS4 and NS5b, and would also conclude that the description of "NS345b-encoding DNA" in Example 11 is due to a typographical error.

First, the Paliard et al. documents stress the fact that NS5a is responsible for inducing an anti-HCV immune response. The invention descriptions teach the importance of NS5a either for priming and/or boosting the immune response against HCV virus. For example, page 15, lines 23-26 of the WO 01/03812 publication states that "polypeptides making up the fusion protein comprise at least one epitope, which is recognized by a T cell receptor on an activated T cell, such as 2152-HEYPVGSQL-2160 (SEQ ID NO:1) and 2224-AELIEANLLWRQEMG-2238 (SEQ ID NO:2)." It is also mentioned at page 15, lines 16-17 of the WO publication that "NS5a occurs at approximately amino acid 1973 to amino acid 2420...". Also, the WO publication states at page 14, lines 5-12 that "[f]usion proteins of the invention (NS3NS4NS5a fusion proteins, also termed "NS345a" herein) comprise HCV NS3, NS4 (NS4a and NS4b), and NS5a polypeptides or comprise HCV NS3, NS4 (NS4a and NS4b), NS5a and NS5b polypeptides (NS3NS4NS5aNS5b fusion proteins, also termed "NS345ab" herein)." The documents do not teach or suggest fusion proteins comprising NS5b but not NS5a.

Second, all of the examples included in the Paliard et al. documents, other than Example 11 (i.e. Examples 1-10 and 12) are clearly directed to the use of NS5a, alone or in combination with other HCV polypeptides. In particular, the $CD4^+$ and $CD8^+$ responses are evaluated with peptides comprising NS5a (see Examples 1-4, and Table 1).

Third, the claims in the '346 patent are directed to fusion proteins comprising NS5a, and methods for using the same. Similarly, the claims in the '539 patent are directed to polynucleotides comprising sequences encoding NS5a, and methods for using the same.

Fourth, Example 11 contains internal discrepancies, as well as variations between the Paliard et al. documents cited by the Examiner. These discrepancies and variations, along

with the disclosure discussed above, make it clear that the "NS345b-encoding DNA" set forth in the example does not refer to an expression vector encoding only NS3NS4 and NS5b, and that this description is due to a typographical error.

Applicants note that Example 11 is entitled "Efficiency of NS345b-encoding DNA Vaccine Formulation to Prime CTLs in Mice." In addition, the text of the example states that "the results demonstrate that priming with plasmid DNA encoding NS345b or PLG-linked NS345b results in activation of $CD8^+$ HCV specific T cells." However, the example does not disclose an expression vector encoding "NS345b." In fact, the protocol states that the mice were immunized with "plasmid DNA encoding NS34b" or with "PLG linked DNA encoding NS5a," followed by "a booster injection of plasmid DNA encoding for NS5a DNA." Thus, from the teaching of the experimental procedure, a skilled artisan would immunize mice with naked DNA coding for NS34b followed by a boost with naked DNA coding for NS5a, or would immunize mice with PLG linked DNA coding for NS5a followed by a boost with naked DNA coding for NS5a. (The intramuscular injection procedure is described in Example 1 and the PLG-linked DNA preparation is described in Example 5.) In other words, according to the protocol the first experiment corresponds to NS34b + NS5a, and the second experiment corresponds to NS5a + NS5a. Furthermore, the results, which are shown in Table 9, indicate in the "NS345 vaccines" column that the vaccines used in the example were "NS345 DNA" and "PLGNS345 DNA" (WO 01/30812 and the '539 patent) or "NS345a DNA" and "PLGNS345 DNA" (the '356 patent). In particular, none of the vaccines are designated "NS345b" vaccines. Finally, in the '346 patent Table 9 is entitled "Efficiency of NS345a-Encoding DNA Vaccine Formulation to Prime CTLs in Mice."

Applicants acknowledge that the internal discrepancies, along with the differences between the various Paliard et al. documents, render Example 11 confusing and difficult to interpret. However, taken together with the disclosures as a whole (as discussed above), a person of ordinary skill in the art would reasonably conclude that the vaccines used in Example 11 certainly included NS5a, whether or not they may have also (contrary to the protocol set forth in the example) included NS5b as well. Thus, the skilled artisan would reasonably conclude that "NS345b" as set forth in Example 11 was due to a typographical error.

In conclusion, Applicants respectfully submit that the Paliard et al. references do not disclose an expression vector as recited in the present claims. Furthermore, the references do not teach or suggest using vectors that comprise NS5b but do not comprise NS5a. Rather, from the teaching of Paliard et al., a person of ordinary skill in the art would reasonably conclude that the NS5a polypeptide is necessary for inducing an HCV immune response.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102/103 rejections.

III. Response to Claim Rejection Under 35 U.S.C. § 101

Claim 28 has been rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter.

In particular, the Examiner has indicated that because the rejected claim does not recite that the microorganism or host cell is "isolated," the claim is improperly directed to a product of nature.

Claim 28 has been amended to recite that the microorganism or host cell is "isolated." Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Response to Claim Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 32 and 34 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to comply with the enablement requirement.

Specifically, the Examiner has stated that the specification does not enable the use of the recited DNA as a vaccine. This rejection is respectfully traversed.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, claims 32 and 34 have been amended to recite an "immunogenic composition" rather than a "pharmaceutical kit comprising a vaccine."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

V. Response to Double Patenting Rejection

Claims 38 and 39 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting as allegedly being unpatentable over claims 10-11 of co-pending U.S. Patent Application No. 11/723,638.

Applicants request that this rejection be held in abeyance until allowable subject matter is indicated.

VI. Conclusion

This response is made without prejudice or disclaimer to any non-elected subject matter, and Applicants reserve the right to file one or more continuation and/or divisional applications directed to any non-elected subject matter.

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: October 21, 2008

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